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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,821	02/18/2005	Degenhard Marx	26581U	1652

34375 7590 05/02/2008

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Alexandria, VA 22314

EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
05/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,821	MARX ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner for this application at the USPTO has changed. Examiner Samira Jean-Louis can be reached at 571-270-3503.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) for foreign priority based on an application filed in Europe on 08/30/2002, which papers have been placed of record in the file.

IDS

The information disclosure statement filed on January 11, 2008 (specifically items DE 4129535) fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but only the abstract information referred to therein been considered.

Response to Amendment

This Office Action is in response to the amendment submitted on 01/11/2008. Claims 1-16 and 18-20 are currently pending in the application, with claim 17 having being cancelled. Accordingly, claims 1-16 and 18-20 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Examiner further acknowledges amendment of claim 15 and consequently the objection has been withdrawn.

Examiner also acknowledges amendment of claim 19 and consequently the rejection under 112 2nd paragraph has also been withdrawn.

Applicant's arguments against the 35 USC 112 2nd paragraph rejection of claim 19 are acknowledged and have been found persuasive. Indeed, in light of the specification, one of ordinary skill would have understood that the ciclesonide stated in the claims refers to the "R" configuration and therefore reference to any other epimers would suggest epimers other than the "R" configuration. In view of the foregoing reasons and applicant's amendment, the rejection under 35 USC 112 2nd paragraph rejection of claim 19 is withdrawn.

Applicant's contention that the previously cited references do not establish a prima facie case of obviousness is acknowledged but is not persuasive. Nagano et al. teaches pharmaceutical compositions of ciclesonide for application to the mucosa that possesses greater mucosal retention of ciclesonide at low osmotic pressures (see col. 3, lines 12-21) through the aid of osmotic pressure controlling agent (see col. 7, claims 5-9), and water insoluble or water low soluble substances such as crystalline cellulose (col. 7, claims 10-11) that are present as solid particles in an aqueous medium (see col.

7, claim 12). This composition of Nagano et al. also contains water soluble polymer substance such as carboxymethyl cellulose (see col. 7, claims 14-15), surfactants (see col. 8, claims 20-22) that can be applied to nasal mucosa (see col. 8, claim 23). While Nagano et al. does not teach the combination of ciclesonide with an antihistamine, Nishibe et al. teaches a pharmaceutical composition for application to mucosa whereby the osmotic pressure of the composition increased mucosal absorption and bioavailability of the medicament (see abstract). Importantly, Nishibe et al. teaches agents for allergies including azelastine hydrochloride as well as steroids for the treatment of rhinitis (i.e. allergic rhinitis; see pg. 3, paragraph 22). Thus, to one of ordinary skill in the art, it would have been obvious to substitute the ciclesonide of Nagano et al. for the steroid of Nishibe et al. in view of the low systemic effects of ciclesonide taught by Nagano et al. Moreover, one of ordinary skill in the art would have predicted successful results since Nishibe et al. taught the combination of a steroid with the instantly claimed antihistamine. As a result, all the limitations of the instant claimed invention have been met and a case for obviousness is established.

However, due to a common assignment of Nagano et al. with the instant claimed invention and in view of applicant's argument with respect to Nagano et al. as being unavailable as a reference, the rejection under 35 U.S. C. 103 (a) is withdrawn.

In view of applicant's amendment, the following modified 112 1rst and 103 (a) Non-Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making pharmaceutically acceptable salts does not reasonably provide enablement for making solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims are drawn to a pharmaceutical composition comprising as active ingredients a combination of at least one antihistamine, or a stereoisomer, a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, and ciclesonide, or a pharmaceutically acceptable salt of ciclesonide, an epimer of ciclesonide, a solvate of ciclesonide, a physiologically functional derivative of ciclesonide or a solvate thereof, and a pharmaceutically acceptable carrier and/or one ore more excipients. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention.

Attention is directed to *In reWands,* 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman,* 230 USPQ 546 (BdApls1986) at 547 the court recited eight factors: (1) the nature of the invention; (2)

the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a pharmaceutical composition comprising as active ingredients a combination of at least one antihistamine, or a stereoisomer, a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, and ciclesonide, or a pharmaceutically acceptable salt of ciclesonide, an epimer of ciclesonide, a solvate of ciclesonide, a physiologically functional derivative of ciclesonide or a solvate thereof, and a pharmaceutically acceptable carrier and/or one ore more excipients. The relative skill of those in the art is high, that of a PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Vippagunta et al. who indicates that predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice is both complex and difficult. All compounds respond differently to possible formation of hydrates. Therefore Vippagunta et al. indicates that generalizations cannot be made for a series of compounds and their respective solvates (see Vippagunta et al., Advanced Drug Delivery Reviews, 2001, Vol. 48, pg. 18, section 3.4) and applicant fails to provide enablement support.

2. The breadth of the claims

The claims are thus very broad insofar as they recite a pharmaceutical composition comprising as active ingredients a combination of at least one antihistamine, or a stereoisomer, a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, and ciclesonide, or a pharmaceutically acceptable salt of ciclesonide, an epimer of ciclesonide, a solvate of ciclesonide, a physiologically functional derivative of ciclesonide or a solvate thereof, and a pharmaceutically acceptable carrier and/or one ore more excipients, yet applicant fails to provide enablement on the synthesis of the solvates of the antihistamine or that of ciclesonide will be accomplished as previously mentioned.

3. The amount of direction or guidance provided and the presence or absence of working examples

The Specification is not adequately enabled as to how to make a hydrate and provides no direction or guidance for a method to synthesize the solvate of the antihistamine or that of ciclesonide. In fact, applicant provided no guidance on how to obtain the aforementioned composition. As a result, countless experimentation would be necessary to obtain the solvates of the antihistamines or that of ciclesonide claimed by applicant.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed solvate of antihistamine or that of ciclesonide could be predictably made as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation in order to obtain the solvates of the aforementioned compounds claimed by applicant, with no assurance of success.

Genentech, 108 F.3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Thus, in the absence of working examples there is no showing that the instant compounds will form solvates. Since it is clear that merely bringing the compound into contact with water does not result in a hydrate , additional direction or guidance is needed to make them and the specification has no such direction or guidance. Therefore, only the chemically structurally defined chemicals, but not the full breadth of the claims meet the enablement requirement provision of 35 USC § 112, first paragraph.

Therefore, a pharmaceutical composition comprising as active ingredients a combination of at least one antihistamine, or a stereoisomer, a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, and ciclesonide,

or a pharmaceutically acceptable salt of ciclesonide, an epimer of ciclesonide, a solvate of ciclesonide, a physiologically functional derivative of ciclesonide or a solvate thereof, and a pharmaceutically acceptable carrier and/or one ore more excipients is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16, 18, and 20 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Magee et al. (U.S. 2002/0111495 A1).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Magee et al. teaches the use of selective PDE4 inhibitors for improved therapeutic treatment of a number of inflammatory, respiratory and allergic diseases including chronic rhinitis (i.e. allergic rhinitis; instant claim 18; see pg. 1, paragraph 0006 and pg. 81, paragraphs 0467-0472). Magee et al. further teaches that the present compounds can be used together in combination with one or more therapeutic agents including antihistaminic H2 receptor antagonists such as azelastine (instant claims 15-16), the steroid ciclesonide and with pharmaceutically carriers (instant claim 1; see pg. 34, paragraph 0218 and pg. 92, paragraph 0570-0571). The compositions of Magee et al. can be administered to humans (instant claim 20; see pg. 76, paragraph 0423). Magee et al. also teaches the route of administration that can critically affect bioavailability, solubility of the active agents and rapid absorption (see pg. 100, paragraph 0677). By carriers, Magee et al. teaches addition of acceptable diluents, adjuvants, vehicles viscosity modifiers and other agents known to the artisan for providing favorable properties to the final pharmaceutical composition including water as a solvent, salts such as sodium chloride for isotonic properties (i.e. osmotic pressure-controlling agent; instant claim 7), cellulose-based substances such as sodium carboxymethylcellulose (i.e. water soluble polymer; instant claims 8-9 and 12), polyethylene glycol as a wetting agent, polyethylene polyoxypropylene block polymer as a surfactant (instant claim 13), emollients, humectants such as glycerin (instant claim 13), surfactants and sugars such as glucose (instant claim 7; see pg. 100-102, paragraphs 0677, 0688 and 0697-0698). Magee et al. further teaches the composition

for intranasal application (i.e. nasal mucosa, instant claim 14, see pg. 104, paragraph 0708).

Magee et al. does not particularly teach a composition with a particular osmotic pressure or a composition containing microcrystalline cellulose as solid particles in an aqueous medium.

However, Magee et al. does teach the inclusion of water-low soluble substance such as cellulose derivatives which encompasses all substances containing cellulose including microcrystalline cellulose which are solid particles before addition to the pharmaceutical composition. Moreover, Magee et al. teaches the use of viscosity modifiers and given that microcrystalline cellulose is a well-known viscosity modifier, one of ordinary skill would readily add such compound as solid particles as to obtain the desired product with the desired osmotic pressure. Additionally, Magee et al. teaches the addition of osmotic pressure controlling agents including glucose and sodium chloride. Consequently, these agents would necessarily affect the osmotic pressure of the composition due to their isotonization properties. Thus, to acquire the desired osmotic pressure for enhancing the bioavailability of the active ingredients as suggested by Magee et al., one of ordinary skill would be motivated to vary the concentration of the osmotic pressure controlling agents in a particular form in the composition.

Moreover, applicant is reminded that a prior art reference may "render obvious" without disclosing a feature of the claimed invention, as long as that missing

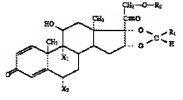
characteristic is necessarily present, or inherent, in the anticipating reference. Please see *Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991)*. Other precedents of the court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. *Please see, e.g., In re Cruciferous Sprout Litig, 301 F.3d 1343, 1351 (Fed. Circ. 2002); MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1366 (Fed. Cir. 1999)* (Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results". In the instant case, the unappreciated osmotic pressure controlling agent property of glucose and sodium chloride does not require recognition by Magee et al.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Magee et al. to treat allergic rhinitis while varying the concentration of the osmotic pressure controlling agents since the motivation of Magee et al. was to provide a composition with enhanced bioavailability and enhanced rate of absorption. Given that Magee et al. teaches a method of treating allergic rhinitis with PDE4 inhibitors, azelastine and ciclesonide with additional excipients, one of ordinary skill would have been motivated to utilize the method of Magee et al. and vary the concentration of water soluble agents and osmotic pressure controlling agents with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition that is readily absorbed.

Claim 19 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Magee et al. (U.S. 2002/0111495 A1) as applied to claims 1-16, 18, and 20 and in further view of Calatayud et al. (U.S. 5,482,934, previously cited by applicant and filed on an IDS 1449).

The Magee et al. reference is as discussed above and incorporated by reference herein. However, Magee et al. does not particularly teach the mixture of the "R" and "S" epimers in a mixing ratio into the composition.

Calatayud et al. teaches compounds of the general formula



with X1 an X2 corresponding to H and R1 is a phenyl group and R2 represents radicals such as C=OCH(CH3)CH3 in the form of an R epimer, S epimer or mixture of the R and S epimers (i.e. ciclesonide) as drugs and/or therapeutic agents (see abstract and col. 3, lines 1-61). Calatayud et al. further teaches that these compounds possess intense pharmacological activity with no or minimal systemic effects (see col. 2 lines 21-23, col. 15, lines 10-11 and col. 16, lines 27-30). Calatayud et al. also teaches synthesis of the mixture of ciclesonide with both the R and S epimers in a ratio of 45/55 of R/S (see col. 11, lines 21-61). Importantly, Calatayud et al. teaches that the mixture of R and S epimers of ciclesonide possess high anti-inflammatory activity, high glucocorticoid activity and high therapeutic index (see col. 17-18, table 2-3 compounds 7-9).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the mixture of epimers of ciclesonide into the composition of Magee et al. to treat allergic rhinitis while varying the concentration of the osmotic pressure controlling agents since the Calatayud et al. teaches that the mixture of epimers possesses intense glucocorticoid activity with minimal systemic effects. Given that Magee et al. teaches a method of treating allergic rhinitis with PDE4 inhibitors, azelastine and ciclesonide with additional excipients, and Calatayud et al. teaches mixtures of epimers of ciclesonide with high glucocorticoid activity and minimal systemic effects, one of ordinary skill would have been motivated to substitute the mixture of epimers of ciclesonide into the composition of Magee et al. with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition that is readily absorbed with no systemic effects.

Claims 1-16, 18, and 20 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Szelenyl et al. (WO 01/22955) in view of Schmidt et al. (J. Clin. Pharmacol. 1999, Vol. 39, pgs. 1062-1069, previously cited by applicant and submitted on an IDS 1449).

WO 01/22955 is the PCT counterpart to U.S. 7,022,687 B1. WO 01/22955 A1 is prior art under U.S.C. 102 (b) as a result of its April 05, 2001 publication date. U.S. 7,022,687 B1 is prior art under U.S.C. 102 (e). Because WO 01/22955 and U.S. 7,022,687 B1 appear to have identical disclosures, the U.S. patent is being used as a

translation of WO 01/22955 PCT. While any reference hereinafter to column and line numbers will be based upon the U.S. patent disclosure, such reference should be interpreted as referring to the corresponding disclosure of the aforementioned PCT counterpart.

Szelenyl et al. teaches the combination of a soft steroid such as loteprednol and at least one antihistamine, such as azelastine and/or levocabastine for the local treatment of allergies and airway disorders including allergic rhinitis (see abstract and col. 6, claims 1-2, 4-5, 8, ; instant claims 1, 15-16, and 18). The administration can be intranasal (instant claim 14; see col. 1, line 66, and col. 2, line 53) and the composition can further include solvents such as water, preservatives, stabilizers such as water soluble polymers such as sodium carboxymethyl-cellulose or mixtures of microcrystalline cellulose and sodium carboxymethylcellulose known as Avicel RC (instant claims 2, 8-9, 11-12), isotonicizing agents such as sodium chloride or glucose (i.e. osmotic pressure controlling agents; instant claim 7), and suitable wetting agents (instant claim 13; col. 4, lines 5-14, 29-33, and 45-67).

Szelenyl et al. does not particularly teach a composition containing ciclesonide. Similarly, Szelenyl et al. does not teach a composition with a particular osmotic pressure or a composition containing microcrystalline cellulose as solid particles in an aqueous medium.

While Szelenyl et al. does not teach particular osmotic pressures, he does teach the addition of water soluble substances along with isotonicizing agents which are solid

particles in nature in the composition which would necessarily affect the osmotic pressure. Thus, it would have been within the purview of the skilled artisan to experiment with varying concentrations of the aforementioned compounds and various forms of the aforementioned products as to obtain the desired product with the desired osmotic pressure.

Schmidt et al. teaches the use of the soft steroid, ciclesonide, as an effective steroid in the treatment of allergic rhinitis without producing local or systemic effects (see abstract). Schmidt et al. further teaches that ciclesonide has an "R" epimer with a higher binding affinity than the "S" epimer to the glucocorticoid receptor (see pg. 1063, left col. paragraph 1). This compound can be administered intranasally (see pg. 1063, right col. paragraph 1) was found to be highly effective in the treatment of allergic rhinitis and led to a rapid alleviation of symptoms without producing systemic side effects (see pg. 1069, left col., last paragraph).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the ciclesonide of Schmidt et al. for the loteprednol of Szelenyl et al. to treat allergic rhinitis since Schmidt et al. teaches that ciclesonide possesses low systemic effects. Moreover, as a general principle it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining them flows logically from their having been

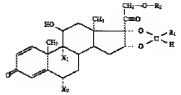
individually taught in the prior art. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06.**

Given that Szelenyl et al. teaches a composition containing a soft steroid and antihistamines for treating allergic rhinitis with additional excipients, and Schmidt et al. teaches that ciclesonide is effective in treating allergic rhinitis without producing local or systemic effects, one of ordinary skill would have been motivated to substitute the ciclesonide of Schmidt et al. for the loteprednol of Szelenyl et al. with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition with minimal side effects.

Claim 19 is rejected under 35 U.S.C. 103 (a) as being unpatentable over unpatentable over Szelenyl et al. (WO 01/22955) in view of Schmidt et al. (J. Clin. Pharmacol. 1999, Vol. 39, pgs. 1062-1069, previously cited by applicant and submitted on an IDS 1449) as applied to claims 1-16, 18, and 20 and in further view of Calatayud et al. (U.S. 5,482,934, previously cited by applicant and filed on an IDS 1449).

The Szelenyl et al. reference is as discussed above and incorporated by reference herein. However, Szelenyl et al. does not particularly teach the mixture of the "R" and "S" epimers in a mixing ratio into the composition.

Calatayud et al. teaches compounds of the general formula



with X1 an X2 corresponding to H and R1 is a phenyl group and R2 represents radicals such as C=OCH(CH3)CH3 in the form of an R epimer, S epimer or mixture of the R and S epimers (i.e. ciclesonide) as drugs and/or therapeutic agents (see abstract and col. 3, lines 1-61). Calatayud et al. further teaches that these compounds possess intense pharmacological activity with no or minimal systemic effects (see col. 2 lines 21-23, col. 15, lines 10-11 and col. 16, lines 27-30). Calatayud et al. also teaches synthesis of the mixture of ciclesonide with both the R and S epimers in a ratio of 45/55 of R/S (see col. 11, lines 21-61). Importantly, Calatayud et al. teaches that the mixture of R and S epimers of ciclesonide possess high anti-inflammatory activity, high glucocorticoid activity and high therapeutic index (see col. 17-18, table 2-3 compounds 7-9).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the mixture of epimers of ciclesonide into the composition of Szelenyl et al. to treat allergic rhinitis since the Calatayud et al. teaches that the mixture of epimers possesses intense glucocorticoid activity with minimal systemic effects. Given that Szelenyl et al. teaches a composition of treating allergic rhinitis with azelastine or levocabastine and a soft steroid along with additional excipients, and Schmidt et al. teaches the use of ciclesonide for treating allergic rhinitis with low systemic effects, and Calatayud et al. teaches mixtures of epimers of ciclesonide with

high glucocorticoid activity and minimal systemic effects, one of ordinary skill would have been motivated to substitute the mixture of epimers of ciclesonide for the "R" epimer into the composition of Szelenyl et al. with the reasonable expectation of providing a composition that is efficacious in treating allergic rhinitis and a composition that possesses no systemic effects.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L./

Examiner, Art Unit 1617

04/18/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617